The brain-specific proteins as potential targets for the treatment of diabetic neuropathy

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Diabetes mellitus (DM) is associated with vitamin deficiency, including vitamin D. Active form of vitamin D3 (1,25(OH)2D3) is well recognized as a neurosteroid that modulates multiple brain functions but precise molecular mechanisms are still unclear.
The study aims to elucidate whether expression of key proteins in diabetic brain areas (cerebral cortex, hippocampus, and cerebellum) is impaired and whether vitamin D3 treatment can correct this. For studies was used a model of type 2 DM induced by a high-fat diet combined with a low-dose STZ injection in male Wistar rats treated for 30 days with or without vitamin D3 (780 IU/kg b.w. per os.). The levels of vascular endothelial growth factor (VEGF), ionized calcium-binding adaptor molecule 1 (Iba-1), zonula occludens-one (ZO-1), and phospho-tau (p-tau) were evaluated by immunoblotting followed by densitometric analysis. DM development was confirmed by hyperglycemia, insulin resistance testing and increasing of body weight compared to control. Vitamin D3 led to partial decrease blood glucose, normalization of 25(OH)D content in blood serum but didn't affect body weight in DM. Blood-brain barrier functioning is dependent on VEGF and ZO-1 protein expressions. DM led to increasing VEGF levels in cortex and hippocampus but Vitamin D3 normalized it only in cortex. Tight junction protein level, ZO-1, was down-regulated in cortex and was normalized by vitamin D3. Iba-1 level, a microglia/macrophage-specific protein, was increased in cortex and hippocampus in DM and vitamin D3 decreased its level. P-tau level, major microtubule-associated protein of a mature neuron, was increased in cortex and cerebellum and partially decreased by vitamin D3 in these areas.
Thus, vitamin D3 can protect key protein levels impaired by DM in investigated brain areas through modulation of angiogenic factors, influencing tight junctions' proteins, regulating the assembly and stability of microtubules in the axons of neurons and microglia state.